α-Acyl-o-tolunitriles as Intermediates in the Preparation of 3-Substituted Isoquinolines and 1-Amino-2-benzopyrylium Derivatives[1]

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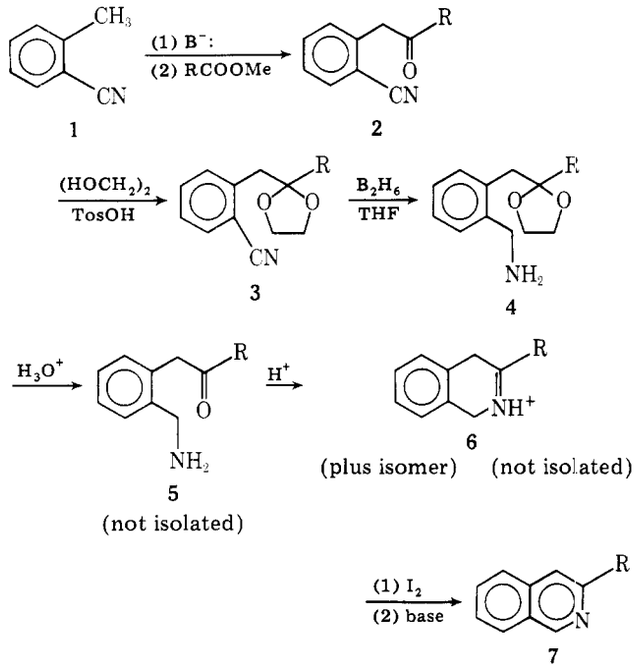
The carbonyl function of α-acyl-o-tolunitriles (**2**) was protected by reaction with ethylene glycol, and the nitrile function of the resulting 1,3-dioxolanyl derivatives (**3**) was reduced to the corresponding benzylamine (**4**). Acid-catalyzed hydrolysis of the protective group of **4** was accompanied by cyclization to afford the easily dehydrogenated 3-substituted dihydroisoquinolines (e.g., **6**). Treatment of α-acyl-o-tolunitriles (**2**) with hydrobromic acid resulted in the first isolation of pure 1-amino-3-aryl-2-benzopyrylium bromides (**10**). These salts (**10**) underwent facile hydrolysis to isocoumarins (**11**) and borohydride reduction (in poor yield) to 3-arylisoquinolines (**7**).

The study of the polar cycloaddition[2,3] of electron-rich olefins with isoquinolinium salts[4] has indicated the importance of having a substituent at position 3 of the isoquinolinium ion, for without such a substituent complicating side reactions may occur. It was also necessary that there be no substituent at position 1. For this particular substitution pattern, the modified Pomeranz-Fritsch[5] appeared more favorable than the other classical isoquinoline syntheses;[6,7] yet at best it afforded only poor overall yield.

A possible alternate approach to such 3-substituted isoquinolines would be the cyclization of benzylamines having an ortho side chain having a carbonyl group at the β position. Although Campbell[8] had suggested that ortho-substituted benzylamines were probably not suitable starting materials for isoquinoline synthesis, it seemed desirable to test this route.

The discovery independently by Boyce and Levine[9] and by Rash, Boatman, and Hauser[10,11] that o-tolunitrile (**1**) can be acylated in the presence of a strong base afforded an easy route



to o-cyanobenzyl ketones (**2**), which differ from the desired benzylamine (**5**) in lacking four hydrogen atoms. The yields in the acylation step averaged about 50% (based upon the ester) using sodium hydride[10,11] or amide[9,12] as the base, the limiting factor appearing to be the known[13] tendency of the anion to undergo condensation with o-tolunitrile.[9-11] The results are recorded in Table I.

Protection of the carbonyl group during the reduction step was achieved by formation of the 1,3-dioxolane derivatives (**3**). While the yields were generally high for dioxolane, formation was slower than usual,[14] and in the case of the *tert*-butyl derivative (**3**; R = *t*-Bu) 11 days of refluxing with ethylene glycol were required to produce a 59% yield (Table II). For the reduction of the nitrile function, lithium aluminum hydride appeared promising since it had been reported[15] to reduce o-tolunitrile to o-methylbenzylamine in 88% yield. Some reduction could be effected by refluxing α-(2-phenyl-1,3-dioxolan-2-yl)-o-tolunitrile (**3a**) with an excess of lithium aluminum hydride, but the yield of amine (**4a**), isolated as the hydrochloride, was only 33%. Better results were obtained with diborane,[16,17] which afforded **4a** hydrochloride in 70.5% yield.

With the exception of **4a** and **4e** (which has the *p*-dimethylaminophenyl substituent), none of the benzylamines (**4**) could be isolated as hydrochlorides, and they were submitted directly to the hydrolysis–cyclization procedure.

It had been anticipated that the acid-catalyzed hydrolysis of the dioxolane ring of the benzylamine (**4a**) would be accompanied by ring closure, affording either 3-phenyl-1,4-dihydroisoquinoline (**6a**) or a mixture containing the 1,2-dihydro analogue. The hydrochloride of **4a** was refluxed for 3 h in methanol containing a small quantity of hydrochloric acid. Addition of base afforded a yellow precipitate which was extracted into $CDCl_3$. The ^1H NMR spectrum of the solution indicated the presence of 3-phenylisoquinoline (**7a**) as well as one or more dihydro derivatives. Air was bubbled through the $CDCl_3$ solution for 10 min and the spectrum reexamined, revealing that signals characteristic of the dihydroisoquinolines had disappeared and only signals remained for aromatic protons with a characteristic singlet at δ 9.93.

Since samples of 3-phenylisoquinoline prepared by the air oxidation method proved difficult to purify and since it is known[18] that iodine will dehydrogenate 1,2-dihydroisoquinolines while air oxidizes them to isocarbostyryls,[19] it seemed likely that iodine would be the most desirable reagent for the dehydrogenation step. When the hydrolysis–cyclization was followed by reaction with iodine, the hydrochloride of the benzylamine (**4a**) afforded 3-phenylisoquinoline in 70% yield. For the preparation of the other 3-substituted isoquinolines, reduction of the nitrile group (**3** → **4**), hydrolysis–cyclization, and dehydrogenation (**4** → **7**) were carried out without purification of the intermediates; the 3-substituted isoquinoline was isolated as a picrate, from which the base is easily recovered. The results, summarized in Table III, show that the overall yields (**4** → **7**) are very similar.

The new synthesis of 3-substituted isoquinolines is clearly superior to known syntheses in overall yield, scope, simplicity, and availability of starting materials.

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Table I. Acylation Products

2, R	registry no.	time, h	yield,[b] %	mp, °C	significant ^{1}H NMR data[a] 2′,6′ H[c,d]	CH_2[e]	misc.
(**a**) C_6H_5	10517-64-3	7	54[f]	110.5–111.5[g]	7.98–8.15 (m)	4.51	
(**b**) *p*-$MeOC_6H_4$	13670-86-5	72	41[f]	96–97[h]	7.97 (J = 9 Hz)	4.45	3.83 (s, Me)
(**c**) *p*-ClC_6H_4	67237-70-1	8	63[f]	94–94.5	7.97 (J = 8.5 Hz)	4.48	
(**d**) *p*-MeC_6H_4	67237-71-2	1	45[i]	101–101.5	8.00 (J = 8 Hz)	4.51	2.39 (s, Me)
(**e**) *p*-$Me_2NC_6H_4$	67237-72-3	1	48[i]	170.5–171.5	7.90 (J = 9 Hz)	4.41	3.02 (s, Me)
(**f**) 3,4-$(MeO)_2C_6H_3$	67237-73-4	1	64[i]	143–143.5	*j*	4.48	3.91 (s, Me), 3.92 (s, Me)
(**g**) 3,4-$(OCH_2O)C_6H_3$	67237-74-5	1	54[i]	132–133	*j*	4.41	5.97 (s, CH_2)
(**h**) Me_3C	67237-75-6	2	37[i]	43.5–44		4.05	1.15 (s, Me)
(**i**) C_2H_5O	67237-76-7	1.8	25[i]	53–53.5		3.83	1.20 (t, Me), 4.16 (q, CH_2)

[a] ^{1}H NMR measurements (δ, $CDCl_3$) using tetramethylsilane as a standard. [b] Yields are based upon the nitrile in the sodium hydride procedure and upon the ester in the amide procedure. The editor has been supplied with acceptable C,H,N analyses for all new compounds (**2c–i**). [c] With the exception of **2a**, in which the 2′,6′ H's appear as a multiplet, all compounds gave signals which (where identifiable) appeared as broad doublets. [d] Other aromatic signals have been omitted. [e] All benzylic methylene signals appeared as singlets. [f] By the sodium hydride procedure. [g] Literature[10] mp 110.5–113 °C. [h] Literature[9] mp 96.0–96.9 °C. [i] Sodium amide procedure. [j] Signals not identified.

Table II. Formation of Dioxolane Derivatives 3

3, R	registry no.	time, h	mp,[a] °C	yield, %	^{1}H NMR[b] CH_2[c]	CH_2CH_2[d]	misc.
(**a**) C_6H_5	37993-73-0	29	103	95	3.40	3.65	
(**b**) *p*-$MeOC_6H_4$	37993-74-1	144	127.5–128.5	86	3.40	3.77	3.75 (s, Me)
(**c**) *p*-ClC_6H_4	67237-77-8	72	103.5–104.5	99	3.35	3.75	
(**d**) *p*-MEC_6H_4	67237-78-9	48	93–94	96	3.42	3.77	2.34 (s, Me)
(**e**) *p*-$Me_2NC_6H_4$	67237-79-0	192	143.5–144	88[e]	3.38	3.74	2.93 (s, Me)
(**f**) 3,4-$(MeO)_2C_6H_3$	67237-80-3	96	112–113	92	3.38	3.82	3.77 (s, Me)
(**g**) 3,4-$(OCH_2O)C_6H_3$	67237-81-4	72	103.5–104	95	3.37	3.75	5.92 (s, CH_2)
(**h**) Me_3C	67237-82-5	264	79.5–80.5	59	3.22	3.00 (t), 3.70 (t)	1.07 (s, Me)

[a] Melting point of analytical sample. The editor has been provided with satisfactory elemental analyses (C,H,N) for all compounds listed. [b] Chemical shifts are in δ ($CDCl_3$) from tetramethylsilane. All aromatic resonances have been omitted. [c] Benzylic methylene groups, all of which appeared as singlets. [d] Except as noted, all signals appeared as singlets. [e] Corrected for recovered ketone.

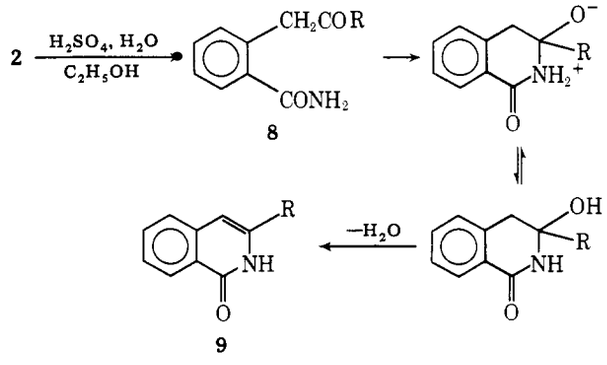
Table III. Conversion of Dioxolanes 3 to 3-Substituted Isoquinoline Picrates and Bases (7)

R	picrate mp, °C	picrate yield, %	picrate registry no.	base mp, °C	base yield, %	base registry no.
(**a**) C_6H_5	197–199	*a*	67237-83-6	102.5–103.5[b]	49[c]	37993-76-3
(**b**) *p*-$MeOC_6H_4$	243[d]	41	67237-84-7	100.5–101.5[e]	86[f]	20435-81-8
(**c**) *p*-ClC_6H_4	243–244[d]	38[g]	67237-86-9	148–148.5	98[f]	67237-85-8
(**d**) *p*-MeC_6H_4	256–257[d]	41	67237-88-1	76–76.5	*h*	67237-87-0
(**f**) 3,4-$(MeO)_2C_6H_3$	238–240[d]	43	67237-90-5	90.5–92.5	87[f]	67237-89-2
(**g**) 3,4-$(OCH_2O)C_6H_3$	244–245[d]	45	67237-92-7	131–131.5	96[f]	67237-91-6
(**h**) Me_3C	156.5–157.5	44[i]	67237-94-9	*j*	93[f]	63144-53-6

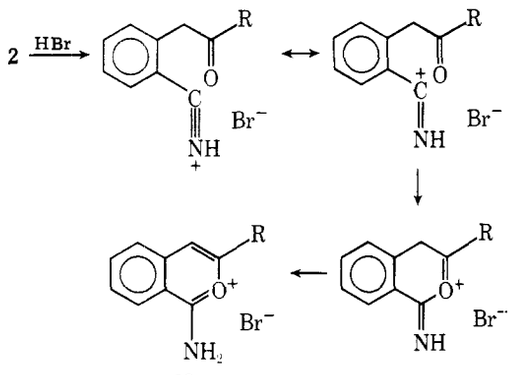
[a] This picrate was obtained from the previously isolated base. It is reported for the purpose of comparison. [b] Literature[20] mp 103–105 °C. [c] This is the overall yield of the base from **3a**. [d] With decomposition. [e] Literature[21] mp 95 °C. [f] Yield from picrate. [g] The borane reduction step was carried out as usual except that 14 days were required at room temperature. [h] Not recorded. [i] The hydrolysis and cyclization step involved a 12-h reflux in methanol–hydrochloric acid. [j] The base, which did not crystallize, was converted to the methiodide, mp 222 °C.

While our method provides the best route from α-acyl-*o*-tolunitriles (**2**) to the isoquinolines, it was demonstrated earlier[9] that the related isocarbostyryls may be prepared from the same starting materials in 82–90% yield by the action of sulfuric acid in 95% ethanol. The mechanism proposed by the earlier authors suggested that the route of the reaction from the nitrile (**2**) to the isocarbostyryl (**9**) passed through the amide **8**.

Experiments carried out here on the α-acyl-*o*-tolunitriles (**2**) using modified Ritter[22] conditions (48% hydrobromic acid at room temperature) gave instead of the isocarbostyryls (**9**) the salts which had the composition expected from the addition of 1 mol of hydrogen bromide to 1 mol of the nitrile (**2**).



From the spectra and reactions of the salts, it seems that these must be 1-amino-3-substituted benzo[c]pyrylium salts (10). For the phenyl derivative (10; R = Ph), the UV absorption spectrum indicated a highly conjugated system, the IR spectrum showed no identifiable carbonyl or nitrile absorptions, and the ^1H NMR spectrum showed signals in the δ 7.53–8.78 region only.



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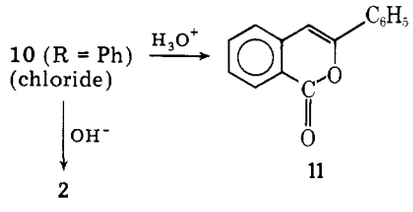
Compound 10 (R = Ph) has never before been isolated in a pure condition, although its existence as a chloride salt had been postulated by Berti[23] as a probable component in an unseparable mixture. Berti's conjecture that it was the 1-amino-3-phenylbenzo[c]pyrylium salt (10; R = Ph) in the mixture which afforded 3-phenylisocoumarin (11) on acid



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hydrolysis and 2-phenacylbenzonitrile (2) on alkaline hydrolysis is fully borne out by our observations on the behavior of pure 10 (R = Ph). It was found that even in the absence of acid the addition of water to a warm solution of the pure pyrylium salt (10; R = Ph) in dimethyl sulfoxide afforded the isocoumarin 11 in 88% yield. The action of aqueous ammonia on the pure pyrylium salt 10 at room temperature for 24 h gave 2-phenacylbenzonitrile (2) in 79% yield. Apparently, proton abstraction followed by reversion to the keto nitrile structure is favored over the formation of 1-amino-3-phenylisoquinoline.

A brief investigation of the action of sodium borohydride in methanol at 0 °C on the 1-amino-3-arylbenzo[c]pyrylium salts showed that a complex mixture containing a small quantity of 3-arylisoquinoline (17%, R = Ph; 29%, R = p-$CH_3OC_6H_4$) was formed, but the major products appeared to be the o-phenacylbenzonitriles (2) or the corresponding secondary alcohols. The reaction appeared to offer little promise as a practical route to isoquinoline derivatives.

Experimental Section

The elemental analyses were performed by M-H-W Laboratories, Garden City, Mich. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. UV absorption spectra were taken with a Beckman Model DB-G spectrophotometer. IR spectra of solids (KBr discs) and liquids (neat) were taken with a Perkin Model 237 spectrometer. ^1H NMR spectra were obtained at 60 MHz with Varian T-60 or A-60 spectrometers using tetramethylsilane as an internal standard.

General Procedures for the Preparation of α-Acyl-o-tolunitriles (2). A. By the Sodium Hydride Procedure. This method is an adaptation of that described by Rash.[11] A stirred slurry of 4 equiv of sodium hydride (57% dispersion in mineral oil) in 1,2-dimethoxyethane (monoglyme) was refluxed under nitrogen. A solution of 1 equiv of o-tolunitrile and 1 equiv of ester in monoglyme was added to the slurry. The mixture was refluxed under nitrogen for 7–72 h (Table I), after which time most of the solvent was removed under reduced pressure. Ether and water were added to the residue. A portion of the product is often ether-insoluble, and this material was isolated by filtration. The ethereal solution in any case was separated and dried. The ether was evaporated and the residue recrystallized from ethanol (Table I).

B. By the Sodium Amide Procedure. This method is an adaptation of that of Boyce and Levine.[9] Sodium amide was prepared by adding 2 equiv of sodium metal to a large excess of anhydrous liquid ammonia with a crystal of ferric nitrate added as catalyst. A solution of 2 equiv of o-tolunitrile in anhydrous ether was added. After sufficient time for anion formation (about 15 min), a solution of 1 equiv of ester was added. The mixture was stirred for 1–2 h (Table I). The reaction was quenched with 2 equiv of ammonium chloride. After evaporation of the ammonia, ether and water were added. Products insoluble in the ether–water mixture were isolated by filtration. Others were obtained from the ether extract, usually by recrystallization.

Preparation of Dioxolane Derivatives (3) of Keto Nitriles (2). In a reflux apparatus provided with a Dean-Stark trap, 0.2 mol of the keto nitrile 2 was dissolved in a mixture of 300 mL of anhydrous benzene and 49.6 g (0.8 mol) of ethylene glycol. p-Toluenesulfonic acid (0.4 g) was added, and the mixture was refluxed until approximately the theoretical quantity of water had been collected (Table II). The benzene solution was washed with bicarbonate solution and water and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residue was pure enough for use in the next step, but it could be recrystallized from ethanol.

Borane Reduction of α-(2-Substituted-1,3-dioxolan-2-yl)-o-tolunitrile (3 → 4). In a three-neck flask equipped with a condenser, drying tube, nitrogen inlet, and an addition funnel was placed 0.02 mol of the dioxolane derivative. After the system had been flushed with nitrogen, 20 mL of 1 M borane in tetrahydrofuran was added and the solution was allowed to stand at room temperature for 24 hr. Then an additional 10 mL of borane–tetrahydrofuran was added, and after 24 h it was quenched by the addition of 30 mL of ethanol. Most of the solvents were removed under reduced pressure, except in the case of 3 (R = Ph) where the crude amine was subjected directly to hydrolysis and cyclization.

***o*-[(2-Phenyl-1,3-dioxolan-2-yl)methyl]benzylamine (4a) Hydrochloride.** The crude amine 4a obtained from nitrile 3a was dissolved in ethanol and precipitated as the salt by passing hydrogen chloride through the solution for 10 min. The colorless precipitate was collected and dried to give 4.3 g (70.5%) of the hydrochloride salt (4a·HCl) in an analytically pure condition: mp 189–190.5 °C; ^1H NMR [$(CD_3)_2SO$] δ 3.25 (s, 2, CH_2), 3.65 (s, 4, CH_2CH_2), 4.05 (s, 2, CH_2N), 7.14–7.60 (m, 9, aromatic), 8.80 (brd s, 3, NH_3^+).

Anal. Calcd for $C_{17}H_{20}ClNO_2$: C, 66.77; H, 6.59; N, 4.58. Found: C, 66.70; H, 6.60; N, 4.40.

Hydrolysis and Cyclization of Benzylamine 4a Hydrochloride. A solution of 2.0 g (0.0066 mol) of the hydrochloride salt of benzylamine 4a was refluxed for 10 min in a mixture containing 20 mL of methanol, 40 mL of water, and 1 mL of hydrochloric acid. The mixture was concentrated under reduced pressure to half volume and then basified with sodium hydroxide solution. The yellow precipitate was taken up in chloroform, and the solution was washed twice with water before adding 35 mL of a 0.2 M solution of iodine in chloroform. The mixture was allowed to stand for 45 min, and then excess iodine was removed by washing the solution with sodium bisulfite solution. Evaporation of the solvent yielded 1.3 g of crude product which on recrystallization from ethanol–water afforded 0.95 g (70%) of 3-phenylisoquinoline, mp 99–102 °C. An analytical sample was recrystallized from ethanol: mp 102.5–103.5 °C (lit.[20] mp 103–105 °C); UV max (95% ethanol) 328, 290, 250 nm.

When the hydrolysis–cyclization was carried out essentially as described above but without the treatment with iodine in chloroform and the ^1H NMR spectrum ($CDCl_3$) of the product was taken immediately, the spectrum was complex: δ 3.10 (brd s, 2), 3.85 (brd t, 2), 4.55 (s, 2), 4.95 (brd t, 2), 5.85 (s, 1), 7.03–8.23 (m), 9.33 (s, 1). Air was bubbled through the ^1H NMR sample for 10 min, and a second spectrum was recorded, δ 7.02–8.17 (m, 14) and 9.27 (s, 1), indicating that the product was almost entirely aromatic.

General Procedure for Hydrolysis, Cyclization, and Aromatization of Ortho-Substituted Benzylamines (4 → 7). The crude amine 4 from the reduction procedure was dissolved in 40 mL of methanol and 4 mL of water, 1 mL of concentrated hydrochloric acid was added, and the mixture was refluxed for 3 h. The solution was concentrated and made basic and the product taken up in ether or

chloroform. The solution was washed with water, 35 mL of a solution of iodine in chloroform was added, and the mixture was allowed to stand for approximately 45 min. Excess iodine was removed by washing the solution with a 5% sodium bisulfite solution. The solvent was removed and the residue taken up in a minimum quantity of ethanol. Addition of an ethanolic solution of picric acid caused the precipitation of the picrate. Analytical samples of the picrates were prepared by crystallization from acetonitrile. The results are summarized in Table III.

1-Amino-3-phenyl-2-benzopyrylium Bromide (10; R = Ph). A. By 48% Hydrobromic Acid. A heterogeneous mixture of 3.0 g (0.014 mol) of powdered α-benzoyl-o-tolunitrile (**2a**) and 90 mL of 48% hydrobromic acid was stirred at room temperature for 72 h. Water (30 mL) was added and the yellow precipitate removed by filtration. The product was dried at 72 °C (0.7 mm) to afford 3.7 g (88%) of **10** (R = Ph), mp 292–294 °C dec. An analytical sample crystallized from anhydrous methanol as yellow needles: mp 292–294 °C dec; UV max (95% ethanol) 360 (sh), 348, 312, 300, 264 (sh), 256, 238 (sh), 220 nm; IR (Nujol) C≡N and C=O absent.

B. By Hydrogen Bromide. A slightly less pure product (mp 288–292 °C) was obtained in 83% yield when dry hydrogen bromide was passed for 20 min through a solution of **2a** in acetic anhydride.

Anal. Calcd for $C_{15}H_{12}BrNO$: C, 59.62; H, 4.00; N, 4.64. Found: C, 59.79; H, 3.97; N, 4.48.

3-Phenylisocoumarin (11). To a solution of 2.0 g of the benzopyrylium derivative **10** (R = Ph) in a minimum quantity of warm dimethyl sulfoxide was added water until cloudiness persisted. On cooling, off-white crystals formed which were collected and dried to afford 1.3 g (88%) of 3-phenylisocoumarin (**11**), mp 81.5–82 °C. Recrystallization from methanol–water gave colorless needles, mp 86–86.5 °C (lit.[24] mp 90–91 °C). A mixture melting point with an authentic sample[25] was undepressed: ^{1}H NMR ($CDCl_3$) δ 8.25 (m, 1, H-8), 7.27–7.93 (m, 8, aromatic), 6.90 (s, 1, H-4).

When α-benzoyl-o-toluic acid[25] was subjected to the same conditions, only the starting material was recovered.

Basic Hydrolysis of the Benzopyrylium Derivative 10 (R = Ph). To 0.5 g of the bromide salt **10** (R = Ph) was added 50 mL of 22% aqueous ammonia, and the mixture was stirred at room temperature for 24 h. An off-white solid, 0.28 g (79%), was collected, and upon recrystallization from ethanol–water it was shown by mixture melting point to be α-benzoyl-o-tolunitrile (**2**; R = Ph). The use of triethylamine instead of ammonia afforded the same product (**2**; R = Ph) in 85% yield.

1-Amino-3-(*p*-methoxyphenyl)-2-benzopyrylium Bromide (10; R = *p*-MeOC$_6$H$_4$). This was prepared as in the case of the prototype **10** (R = Ph) (85% yield) by the use of hydrobromic acid: mp 278–279 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.87 (s, 3, Me), 7.11 (brd d, 2, J = 8.5 Hz, H-3′ and H-5′), 7.68–8.15 (m, 8, NH_2 and aryl H), 8.51 (m, 1, OH).

Anal. Calcd for $C_{16}H_{14}BrNO_2$: C, 57.85; H, 4.25; N, 4.22. Found: C, 58.07; H, 4.01; N, 3.97.

Hydrolysis of the salt (**10**; R = *p*-MEOC$_6$H$_4$) was carried out as in the case of the prototype (R = Ph), affording 3-(*p*-methoxyphenyl)-isocoumarin in 84% yield: mp (pure) 119–121 °C (lit.[26] mp 116–122 °C); ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 3, OCH_3), 6.78 (s, 1, H-4), 6.93 (brd d, 2, H-3′ and H-5′), 7.27–7.87 (m, 5, aromatic), 8.18–8.35 (m, 1, H-8).

1-Amino-3-(3′,4′-dimethoxyphenyl)-2-benzopyrylium Bromide (10; R = 3′,4′-(MeO)$_2$C$_6$H$_3$). This was prepared (94% yield) as in the case of the analogues **10**: mp 269.5 °C dec; ^{1}H NMR (Me_2SO-d_6) δ 3.85 (s, 3, Me), 3.89 (s, 3, Me), 7.12 (d, 1, J = 8 Hz, H-5′), 7.57–8.05 (m, 8, NH_2 and aromatic), 8.45–8.62 (m, 1, H-8).

Anal. Calcd for $C_{17}H_{16}BrNO_3$: C, 56.37; H, 4.45; N, 3.87. Found: C, 56.19; H, 4.55; N, 3.68.

Hydrolysis of the salt (**10**; R = 3′,4′-(MeO)$_2$C$_6$H$_3$) was carried out as in the case of the analogues, affording 3-(3′4′-dimethoxyphenyl)-isocoumarin in 95% yield: mp 116 °C (lit.[27] mp 119 °C); ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3, OCH_3), 3.95 (s, 3, OCH_3), 6.80 (s, 1, H-4), 6.9 (d, 1, H-5′), 7.17–7.73 (m, 5, aromatic), 8.20–8.37 (m, 1, H-8).

Reduction of 1-Amino-3-phenyl-2-benzopyrylium Bromide (10; R = Ph). Addition of a solution of 0.062 g (1.7 mmol) of sodium borohydride in 20 mL of anhydrous methanol to an ice–cold solution of 1 g of **10** (R = Ph) in 75 mL of methanol was carried out dropwise. The resulting mixture was kept in an ice bath for 2 h at room temperature for 1 h. Most of the methanol was removed under vacuum, a little water was added, and the organic fraction was taken up in ether. The ethereal solution was evaporated, the residue taken up in ethanol, and an ethanol solution of picric acid added. The picrate of 3-phenylisoquinoline (0.25 g, 17%) crystallized, mp 196–197 °C (melting point was undepressed when mixed with an authentic sample).

Reduction of 1-Amino-3-(*p*-methoxyphenyl)-2-benzopyrylium Bromide (10; R = *p*-MeOC$_6$H$_4$). When the *p*-methoxyphenyl salt (**10**; R = *p*-MeOC$_6$H$_4$) was reduced, 3-(*p*-methoxyphenyl)isoquinoline (**7b**) was isolated as the picrate (29% yield), mp 233–235 °C. Recrystallized from acetonitrile, it gave no depression in a mixture melting point with an authentic sample, mp 240–242 °C.

Registry No.—**1**, 529-19-1; **4a**, 37993-75-2; **4a**·HCl, 67237-95-0; **4b**, 67237-96-1; **4c**, 67237-97-2; **4d**, 67237-98-3; **4e**, 67237-99-4; **4f**, 67238-00-0; **4g**, 67238-01-1; **4h**, 67238-02-2; **10** (R = Ph), 67238-03-3; **10** (R = *p*-MeOC$_6$H$_4$), 67238-04-4; **10** (R = 3′,4′-(MeO)$_2$C$_6$H$_3$), 67238-05-5; **11**, 4809-08-9; RCOOMe (R = C$_6$H$_5$), 93-58-3; RCOOMe (R = *p*-MeOC$_6$H$_4$), 121-98-2; RCOOMe (R = *p*-ClC$_6$H$_4$), 1126-46-1; RCOOMe (R = *p*-MeC$_6$H$_4$), 99-75-2; RCOOMe (R = *p*-Me$_2$NC$_6$H$_4$), 1202-25-1; RCOOMe (R = 3,4-(MeO)$_2$C$_6$H$_3$), 2150-38-1; RCOOMe (R = 3,4-(OCH$_2$O)C$_6$H$_3$), 326-56-7; RCOOMe (R = Me$_3$C), 598-98-1; RCOOMe (R = C$_2$H$_5$O), 623-53-0; ethylene glycol, 107-21-1; 3-(*p*-methoxyphenyl)isocoumarin, 29910-92-7; 3-(3′,4′-dimethoxyphenyl)isocoumarin, 22073-92-3.

References and Notes

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